UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,829	12/19/2007	David R. Tabatadze	24028-015 NATL	8389

7590 09/13/2011

Beattie, Ingrid A.
Mintz, Levin, Cohn, Ferris, Glovsky and Popeo
One Financial Center
Boston, MA 02111

EXAMINER	
KETTER, JAMES S	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
09/13/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,829	TABATADZE ET AL.	
	Examiner	Art Unit	
	JAMES KETTER	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-26* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☒ Claim(s) *26* is/are allowed.

7)☒ Claim(s) *1-25* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *28 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/GB/08) Paper No(s)/Mail Date *6/22/2011*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Upon reconsideration of the claimed invention and the previously cited prior art, a new ground of rejection is presented below. The delay in presenting the rejection is regretted.

Claim 26 is allowed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in the instant rejection:

The nature of the invention. The invention makes use of the insertion of the recited double stranded RNA (dsRNA) molecules into a cell in situ to repair an RNA to which said dsRNA corresponds in part. More narrowly, the repair of CFTR mRNA, to treat cystic fibrosis, is claimed.

The state of the art, and the relative level of skill in the art. Nucleic acid therapies in general were not sufficiently developed at the time of filing to have permitted one of skill to have practiced the claimed invention. Therapies using dsRNA were not routinely used at that time. Sioud (U, newly cited) provides an overview of the phenomenon of RNA interference, and teaches at, e.g., page 154, first and second full paragraphs of the left-hand column, of the IFN

effect in response to dsRNAs, as well as the problem of unintended effcts. Furthermore, the presence of the dsRNA in the cell would tend to REDUCE expression of the target mRNA, which is the opposite effect from that desired. Section 2., "Immunity" of Sioud sets forth the effects in greater detail. Sioud concludes, e.g., at page 161, at the paragraph bridging the columns, that there are and were "issues of delivery and specificity are major obstacles before siRNAs can be used in patients." Furthermore, cystic fibrosis gene therapy was not being practiced successfully at that time, as shown by Pickles (V, newly cited.) For example, Pickles teaches at the paragraph bridging pages 304 and 305 that the glycocalyx is a barrier preventing access of a reagent to the luminal surface. At page 303, in the section bridging the left- and right-hand columns, it is taught that the complexity of the relevant target tissues for such therapy is high, complicating such treatment, as well.

The amount of direction or guidance presented in the specification, and the presence or absence of working examples. The specification does not explain how to avoid the problems known to occur in dsRNA therapies, nor does it set forth routes of administration or treatment protocols to have taught one of skill how to successfully treat any condition, including cystic fibrosis. No working examples are set forth, either.

The breadth of the claims. The claims are drawn to a broad range of possible dsRNA molecules for treatment, particularly so in claims 1-14, which are generic for any disease. Even in the claims drawn to treatment of cystic fibrosis, there is significant breadth in routes and protocols of administration, structures of dsRNA molecules and modifications to said molecules.

The predictability or unpredictability of the art. The pharmaceutical art, particularly involving treatment with biological macromolecules, is and was generally recognized as

unpredictable. There is evidence of failure in the particular art applicable to the instant invention, and no countervailing evidence of success.

The quantity of experimentation. The nature of experimentation where patients are treated with a pharmaceutical to determine its effectiveness, particularly in the present case where no simpler or easier model system is accepted, is such that a large amount of elaborate experimentation is required.

Conclusion. Were the skilled practitioner to have attempted to treat a genetic condition by repairing mRNA, more narrowly cystic fibrosis, said practitioner first would have turned to the specification for guidance in preparing and administering the dsRNA of the invention. However, as set forth above, the specification was deficient in providing the necessary teachings. Next, the skilled practitioner would have turned to the prior art for such guidance, but again, as set forth above, the prior art did not provide solutions to the technical problems known to exist, and instead merely provided teachings pointing out such technical problems. Finally, the skilled practitioner would have turned to empirical experimentation to find a successful dsRNA composition to employ and a protocol to administer it successfully. However, for reasons set forth above, such experimentation in the absence of sufficient guidance from either the specification or the prior art, in the face of a technically immature and unpredictable art, particularly across the breadth of all genetic diseases, requiring significant experimentation to determine success, would have been deemed undue experimentation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James S. Ketter whose telephone number is 571-272-0770. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JSK
12 September 2011

/James S. Ketter/
Primary Examiner, Art Unit 1636